

1 1. A method for diagnosing a malignant neoplasm in a
2 mammal, comprising contacting a bodily fluid from said
3 mammal with an antibody which binds to an human aspartyl
4 (asparaginyl) beta-hydroxylase (HAAH) polypeptide under
5 conditions sufficient to form an antigen-antibody complex
6 and detecting the antigen-antibody complex.

1 2. The method of claim 1, wherein said neoplasm is
2 derived from endodermal tissue.

1 3. The method of claim 1, wherein said neoplasm is
2 selected from the group consisting of colon cancer, breast
3 cancer, pancreatic cancer, liver cancer, and cancer of the
4 bile ducts.

1 4. The method of claim 1, wherein said neoplasm is
2 a cancer of the central nervous system (CNS).

1 5. The method of claim 1, wherein said bodily fluid
2 is selected from the group consisting of a CNS-derived
3 bodily fluid, blood, serum, urine, saliva, sputum, lung
4 effusion, and ascites fluid.

1 6. The method of claim 1, wherein said antibody is a
2 monoclonal antibody.

1 7. The method of claim 6, wherein said monoclonal
2 antibody is FB50.

1 8. The method of claim 6, wherein said monoclonal
2 antibody is selected from the group consisting of 5C7, 5E9,
3 19B, 48A, 74A, 78A, 86A.

1 9. A method for prognosis of a malignant neoplasm
2 of a mammal, comprising
3 (a) contacting a bodily fluid from said mammal
4 with an antibody which binds to an HAAH polypeptide under
5 conditions sufficient to form an antigen-antibody complex
6 and detecting the antigen-antibody complex;
7 (b) quantitating the amount of complex to
8 determine the level of HAAH in said fluid; and
9 (c) comparing the level of HAAH in said fluid
10 with a normal control level of HAAH, wherein increasing
11 levels of HAAH over time indicates an adverse prognosis.

1 10. A method of inhibiting tumor growth in a mammal
2 comprising administering to said mammal a compound which
3 inhibits expression of HAAH.

1 11. The method of claim 10, wherein said compound is
2 a HAAH antisense nucleic acid.

1 12. The method of claim 10, wherein said compound
2 is a ribozyme.

1 13. The method of claim 10, wherein said tumor is
2 derived from endodermal tissue.

1 14. The method of claim 10, wherein said tumor is
2 selected from the group consisting of colon cancer, breast
3 cancer, pancreatic cancer, liver cancer, and cancer of the
4 bile ducts.

1 15. The method of claim 10, wherein said tumor is a
2 CNS tumor.

1 16. A method of inhibiting tumor growth in a mammal
2 comprising administering to said mammal a compound which
3 inhibits an enzymatic activity of HAAH. ? only 1

1 17. The method of claim 16, wherein said enzymatic
2 activity is hydroxylase activity.

1 18. The method of claim 16, wherein said compound
2 is a dominant negative mutant of HAAH.

1 19. The method of claim 18, wherein said dominant
2 negative mutant HAAH comprises a mutation in a catalytic
3 domain of HAAH.

1 20. The method of claim 16, wherein said compound
2 is an HAAH-specific intrabody.

1 21. The method of claim 16, wherein said compound
2 is L-mimosine.

1 22. The method of claim 16, wherein said compound
2 is a hydroxypyridone.

1 23. A method of inhibiting tumor growth in a mammal
2 comprising administering to said mammal a compound which
3 inhibits signal transduction through the IRS signal
4 transduction pathway.

1 24. The method of claim 23, wherein said compound
2 inhibits IRS phosphorylation.

1 25. The method of claim 23, wherein said compound
2 inhibits binding of Fos or Jun to an HAAH promoter sequence.

1 26. A method of inhibiting tumor growth in a mammal
2 comprising administering to said mammal a compound which
3 inhibits HAAH hydroxylation of a NOTCH polypeptide.

1 27. The method of claim 26, wherein said compound
2 inhibits hydroxylation of an EGF-like repeat sequence in a
3 NOTCH polypeptide.

1 28. A method of killing a tumor cell comprising
2 contacting said tumor cell with cytotoxic agent linked to an
3 HAAH-specific antibody.

1 29. A monoclonal antibody that binds to an epitope
2 of HAAH.

1 30. The antibody of claim 29, wherein said epitope
2 is within a catalytic site of HAAH.

1 31. The antibody of claim 29, wherein said
2 monoclonal antibody is selected from the group consisting of
3 5C7, 5E9, 19B, 48A, 74A, 78A, 86A.

1 32. The antibody of claim 29, wherein said
2 monoclonal antibody is selected from the group consisting of
3 HA238A, HA221, HA239, HA241, HA329, or HA355.

1 33. A composition comprising a monoclonal antibody
2 that binds to an epitope of HAAH linked to a cytotoxic
3 agent, wherein said composition preferentially kills tumor
4 cells compared to non-tumor cells.

1 34. A kit for diagnosis of a tumor in a mammal,
2 comprising the antibody of claim 29.

1 35. The kit of claim 34, wherein said antibody is
2 immobilized on a solid phase.

1 36. The kit of claim 35, wherein said solid phase
2 is selected from a group consisting of an assay plate, an
3 assay well, a nitrocellulose membrane, a bead, a dipstick,
4 and a component of an elution column.

1 37. A method of determining whether a candidate
2 compound inhibits HAAH enzymatic activity, comprising
3 (a) providing a HAAH polypeptide;
4 (b) providing a polypeptide comprising an EGF-like
5 domain;
6 (c) contacting said HAAH polypeptide or said NOTCH
7 polypeptide with said candidate compound;
8 (d) determining hydroxylation of said polypeptide of
9 step (b), wherein a decrease in hydroxylation in the
10 presence of said candidate compound compared to that in the
11 absence of said compound indicates that said compound
12 inhibits HAAH enzymatic activity.

1 38. A method of determining whether a candidate
2 compound inhibits HAAH activation of NOTCH, comprising
3 (a) providing a cell expressing HAAH;
4 (b) contacting said cell with a candidate compound;
5 and
6 (c) measuring translocation of activated NOTCH to
7 the nucleus of said cell, wherein a decrease in
8 translocation in the presence of said compound compared to
9 that in the absence of said compound indicates that said
10 compound HAAH activation of NOTCH.

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